Brief Report

Manifestations of Severe Vitamin D Deficiency in Adolescents: Effects of Intramuscular Injection of a Megadose of Cholecalciferol

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Summary

We recorded the manifestations of severe vitamin D deficiency (VDD) in 40 adolescents before and 3 and 6 months after treatment with a mega dose of cholecalciferol (10 000 IU kg\(^{-1}\), max 600 000 IU). Significant improvement of symptoms related to VDD was reported in 34/40. Three months after the injection, serum calcium, phosphate, alkaline phosphatase and parathormone were normal in all adolescents with VDD with 25-hydroxyvitamin D (25OHD) level \(\geq 20\) ng ml\(^{-1}\). After 6 months, the majority had 25OHD level \(< 20\) ng ml\(^{-1}\). Two patterns of radiological changes have been recorded with complete healing achieved in all patients after a year of therapy. A mega dose of cholecalciferol is an effective therapy for treatment of VDD in adolescents for 3 months but not for 6 months. Radiographs of the ends of long bones are still valuable tool for diagnosis and follow-up of these patients.

Key words: Vitamin D Deficiency (VDD), adolescents, radiology.

Introduction

High prevalence of vitamin D deficiency (VDD) is reported from all over the world even in sunny places especially during the winter [1, 2]. Vitamin D is important for musculoskeletal health, particularly in girls during pubertal growth. Optimal intestinal Ca absorption occurs at a serum 25-hydroxyvitamin D (25OHD) concentration of approximately 32 ng ml\(^{-1}\). VDD leads to secondary hyperparathyroidism and increased bone turnover. The clinical spectrum ranges from subclinical to frank deficiency with levels \(< 20\) ng dl\(^{-1}\) [1–8]. In prolonged and/or severe cases, manifestations of rickets/osteomalacia evolve [9, 10]. Asymptomatic adolescents with VDD have high risk of developing hyperparathyroidism with failure to achieve peak bone mass, bone loss and increased risk of fractures [1, 4, 8, 11].

The aims of this study were to investigate the magnitude of VDD in a random sample of adolescents, describe the clinical picture in adolescents with severe VDD (25OHD \(< 10\) ng ml\(^{-1}\) ) and monitor the effects of treatment with a mega dose of intramuscular (IM) cholecalciferol. Forty children with severe VDD were used as controls.

Patients and Methods

In this prospective study, 100 adolescents attending the general practitioner (GP) clinic for checkup were randomly selected to assess the prevalence of VDD. Those with severe VDD (25OHD \(< 10\) ng ml\(^{-1}\) ) were referred to the Endocrine Clinic at Hamad Medical Centre, Doha, Qatar, between October 2005 and October 2006. Detailed history taking and full clinical examination were performed. Laboratory investigations included measuring serum creatinine, Ca, PO4, insulin-like growth factor-I (IGF-I) [radio-immunoassay (RIA)], 25OHD (RIA) and parathormone (PTH) (intact molecule) (RIA) concentrations. A routine radiological film of the wrist or knee was obtained. Patients with VDD were treated with an intramuscular injection of cholecalciferol [10 000 U kg\(^{-1}\), max 600 000 IU (15 mg)]. During each clinic visit, every 2–3 months, the anthropometric and radiological parameters were reassessed and recorded and the laboratory tests repeated.
In 100 randomly selected adolescents (60 females, 40 males), 62 had VDD (25OHD <20 ng ml⁻¹) and 40 had severe VDD (25OHD <10 ng ml⁻¹). They presented with pain in weight bearing joints, back, thighs and/or calves (32/40), difficulty in walking and/or climbing stairs and/or running (9/40), muscle cramps (12/40), facial twitches (4/40) and carpo-pedal spasms (2/40).

Serum PO₄ concentration was significantly lower and PTH and alkaline phosphatase (ALP) concentrations higher in children vs. adolescents with VDD (Table 1). One mega dose injection maintained higher in children vs. adolescents with VDD and PTH and alkaline phosphatase (ALP) concentrations. Carpo-pedal spasms (2/40).

Muscle cramps (12/40), facial twitches (4/40) and thighs and/or calves (32/40), difficulty in walking presented with pain in weight bearing joints, back, No cupping or fraying of the metaphyses was identified. Tensions, widening of the metaphyseal zone with relative more lucency (loss of all bone trabeculations). Prominent primary and secondary bone trabeculae appears as generalized diminished bone density with metabolic bone disease and absence of hypocalcemic episodes (two patients with pattern II had symptomatic hypocalcemia). This can be explained by their relatively larger bone mass (Ca and PO₄ stores) and lower requirement for calcium and PO₄ kg⁻¹ due to relatively slower growth rate compared with infants and young children [12].

Complete healing of the radiological signs of rickets was achieved in the majority (24/26) of adolescents within 6–12 months (Fig. 1). A study of bone histomorphometric changes in 28 patients with osteomalacia treated with vitamin D and calcium showed a significant reduction in osteoid volume and an increase in mineralized bone volume in cortical and trabecular bone after therapy [13]. A meta-analysis showed significant increases in lumbar spine bone mineral density after a year of therapy [14].

Two different radiological patterns of severe VDD in adolescents (n = 26) have been detected. Pattern I, with localized metaphyseal multilocular cystic lesions, occurred in overweight adolescents with good intake of milk/milk products. Whereas pattern II, with generalized diminished bone density, occurred in adolescents with relatively lower body mass index (BMI) (<18), with no or poor intake of milk and lower IGF-I vs. those with pattern I. Adolescents with pattern I appear to have better adaptation to VDD because of maintaining near-normal bone architecture of the cortex of long bones (better bone mass) and having higher serum PO₄ concentrations and absence of hypocalcemic episodes (two patients with pattern II had symptomatic hypocalcemia). This can be explained by their higher fat mass (BMI >25), IGF-I concentrations and consumption of milk (better calcium and phosphate intake). All these factors have been shown to maintain bone density in children and adolescents [15–18] (Table 2).

### Table 1

<table>
<thead>
<tr>
<th>Adolescent with VDD</th>
<th>Before treatment, n = 40</th>
<th>After treatment, n = 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO₄ mmol⁻¹</td>
<td>1.4 ± 0.5</td>
<td>1.7 ± 0.4*</td>
</tr>
<tr>
<td>Ca mmol⁻¹</td>
<td>2.1 ± 0.3</td>
<td>2.3 ± 0.1*</td>
</tr>
<tr>
<td>ALP UI⁻¹</td>
<td>404 ± 212</td>
<td>212 ± 69*</td>
</tr>
<tr>
<td>25OHD ng ml⁻¹</td>
<td>9.3 ± 4.6</td>
<td>27.7 ± 9.2*</td>
</tr>
<tr>
<td>PTH pg ml⁻¹</td>
<td>122.9 ± 55.5</td>
<td>24.8 ± 9.58</td>
</tr>
<tr>
<td>IGF-I ng ml⁻¹</td>
<td>166 ± 45</td>
<td>203 ± 55*</td>
</tr>
</tbody>
</table>

*p < 0.05 after vs. before treatment.
FIG. 1. (A–C) Radiological changes in adolescents with VDD. (A, pattern I) With metaphyseal multilocular cystic lesions which have sclerotic margins at subcortical location without significant cortical erosions, periosteal reaction, osteoporosis or other metaphyseal manifestations. (B, pattern II) With generalized diminished bone density with widening and significant lucency (zone of poor ossification) of the metaphyseal zone with rather loss of all bone trabeculation and osteoporosis of the diaphysis of long bones and the apophyses of ischial bone and iliac. (C) Radiological changes before vs. 6 months after treatment in an adolescent.
In conclusion, even in sunny climates, adolescents may be at risk of VDD. A mega dose of cholecalciferol is an effective therapy for the treatment of VDD in adolescents for 3 months.

References